CASE REPORT

Adult-onset Still's disease presenting as myopericarditis

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SUMMARY

A 24-year-old man presented to the emergency department with fever, maculopapular rash, myalgia and polyarthralgia, thoracic pain and dry cough, which had been present for 24 h. At the time of observation he had high fever (39°C), maculopapular rash on the torso, arms and legs proximally, axillary adenopathies and pharyngitis. Laboratorial data showed elevated inflammation markers (leukocytosis, C reactive protein of 44 mg/dL, erythrocyte sedimentation rate of 120 mm), elevated transaminases, lactate dehydrogenase, ferritin levels (>2000 ng/mL) and rising troponin. ECG had sinus rhythm and ST elevation in leads V1–V5. Thoracic radiography revealed bilateral interstitial infiltrate confirmed by CT scan. Echocardiographic findings included diffuse hypokinesia of the left ventricle and impaired systolic function. After the investigation of an infectious or autoimmune aetiology was negative, the diagnosis of adult-onset Still's disease was considered. The patient was put on a 60 mg/day prednisolone regimen with remission of symptoms and normalisation of systolic function and ECG.

BACKGROUND

Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder of unknown aetiology. The disease typically affects young adults and is characterised by spiking fever, arthralgia and an evanescent rash with other manifestations including pharyngitis, serositis and leukocytosis. Myopericarditis is rare but may result in cardiac failure or arrhythmia. Diagnosis is usually clinical and made after other diseases with similar features are excluded.¹

We think that AOSD should be in the differential diagnosis of myopericarditis, especially those with high ferritin levels.

CASE PRESENTATION

A 24-year-old man presented to the emergency department with fever, maculopapular rash, myalgia, polyarthralgia, thoracic pain and dry cough starting 24 h before. The fever was 39–40°C, hectic, with a weak response to antipyretics, associated with myalgia mainly localised on the back and legs and symmetric polyarthralgia predominantly on small distal joints. The rash intensified with fever and hot water. Chest pain was pleuritic in its characteristics, accompanied by dry cough. The patient denied other respiratory symptoms, nausea, vomiting, diarrhoea, genital ulcers or urinary-tract symptoms, as well as a history of insect bites.

The patient was born in Brazil but had moved to Portugal 5 years before. He was employed in

construction field and lived in the city. He had no animals and had not travelled since he left his country. He did not take any medication, neither did he drink or smoke. No history of drug allergy was reported. Family history was irrelevant.

At admission to our hospital he was febrile (39.2°C) but felt otherwise well, had normal blood pressure and a heart rate of 110 ppm. A maculopapular rash was evident on the trunk, arms and legs proximally and was evanescent. The oropharynx was hyperaemic but had no exudates. Axillary adenopathies were palpable. Heart sounds were rhythmic with no murmur or pericardial friction. Lung sounds were rude on both bases but no adventitious sounds were present. The abdomen had no masses or hepatosplenomegaly. Joint examination revealed neither synovitis nor arthritis.

INVESTIGATIONS

In order to investigate the aetiology, laboratory tests were performed, revealing a haemoglobin of 12.1 g/dL with normocytosis; leukocytosis of 30 000 cells/μL with neutrophilia (90%), elevated α fraction of serum protein electrophoresis, C reactive protein (40 mg/dL), erythrocyte sedimentation rate (ESR) (120 mm 1st h), lactate dehydrogenase (1304 IU/L) and ferritin levels (above 2000 ng/mL). Myocardial involvement was evident by serial elevated troponin T (1.33 μg/L), creatine phosphokinase (CPK) (795 IU/L) and CPK-MB (54 IU/L), with no liver or renal abnormalities. Arterial blood gases were unremarkable. Complement was normal.

ECG showed sinus rhythm, 90 ppm, elevated ST segment with upward concavity on leads V1–V5, I, II and aVL. Transthoracic echocardiography revealed an undilated diffusely hypokinetic left ventricle, with depression of global systolic function (ejection fraction of 43%) and diastolic dysfunction grade I. Chest radiography revealed diffuse, bilateral, interstitial-micronodular infiltrates that were confirmed by thoracic CT. Joint radiography of hands, feet and tibiotarsic showed no erosion.

Extensive investigation was conducted regarding infectious aetiologies: blood cultures were negative; serology to viral hepatitis (hepatitis B virus, hepatitis C virus, hepatitis A virus), HIV (including p24 antigen detection), rapid plasmonic reagin, *Rickettsia conorii*, *Coxiella burnetii*, *Borrelia burgdorferi*, *Mycoplasma pneumoniae*, *Toxoplasma gondii*, Parvovirus B19 and *Leptospira interrogans* antigenuria were all negative; Epstein-Barr virus (EBV) and cytomegalovirus (CMV) displayed a serological pattern of past infection.

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Negative antinuclear antibodies (ANAs), anti-double-stranded DNA (dsDNA), antineutrophil cytoplasmic antibodies (ANCAs), RF and anticitrulline antibodies excluded autoimmunity.

DIFFERENTIAL DIAGNOSIS

The main diagnostic hypotheses for fever and rash with joint and heart involvement are the following:

- HIV primoinfection;
- Mononucleosis syndrome either by EBV or CMV;
- Other viral aetiologies such as coxsackie or enterovirus; although we could not exclude it, prominent inflammatory biomarkers were more suggestive of bacterial infection and arthritis is not common;
- 'Atypical' pneumonia to *Mycoplasma* spp;
- Q fever;
- Mediterranean spotted fever;
- Lyme disease;
- Leptospirosis;
- Secondary syphilis;
- Sarcoidosis: adenopathic and lung involvement are more prominent in those cases;
- Granulomatous diseases such as granulomatosis with polyangiitis or eosinophilia with granulomatous polyangiitis, usually has a subacute presentation on a chronic background of rhinosinusitis, cough and wheezing which was not present;
- Connective tissue diseases such as systemic lupus erythematosus flare, although rare in the absence of ANAs and normal complement;
- Rheumatoid arthritis: joint affection typically occurs with arthritis but rash is not common.

TREATMENT

An empirical antibiotic regimen of ceftriaxone 2 g once a day and clarithromycin 500 mg twice daily was implemented on the first day to cover potential bacterial pathogens. After negative microbiological and serological studies at the seventh day, we admitted AOSD with myopericardial involvement, stopped all antibiotics and started prednisolone 60 mg once a day.

OUTCOME AND FOLLOW-UP

Even before the onset of prednisolone treatment, defervescence had started at day 5, the rash had become more evanescent and thoracic pain and cough had disappeared. Bilateral metacarpophalangeal and tibiotarsal arthritis had developed in the meantime, but remission was accomplished with corticoid therapy. ECG changes and cardiac enzymes normalised within a week and the left ventricle systolic function had improved (ejection fraction 63%) upon echocardiogram evaluation at 2 weeks.

The patient was discharged 2 weeks after the admission and slow corticoid withdrawal was started. When he reached the dose of 15 mg a recrudescence of polyarthritis was noted, leading to the initiation of methotrexate, which was titrated until the dose of 15 mg/week. The patient has been in full remission ever since, with normal ESR and ferritin levels.

MRI was made 6 weeks later and revealed no changes in neither myocardial nor pericardial tissue and the left ventricle systolic function was normal.

DISCUSSION

The diagnosis of AOSD in this patient was based on high-spiking fevers, characteristic evanescent rash which worsened with fever and hot water, polyarthritis, pharyngitis, adenopathies, serositis and elevated inflammatory parameters, including ferritin. There is no specific test or combination of tests that can

be used to establish the diagnosis of AOSD. The Japanese criteria, often termed the Yamaguchi criteria, have the highest sensitivity in patients with a definite diagnosis of AOSD, which require the presence of five features, with at least two being major diagnostic criteria.² There are four major Yamaguchi criteria: fever of at least 39°C (102.2°F) lasting for at least 1 week; arthralgia or arthritis lasting for 2 weeks or longer; a non-pruritic macular or maculopapular skin rash that is salmon-coloured in appearance and that is usually found over the trunk or extremities during febrile episodes; leukocytosis (10 000/μL or greater), with at least 80% granulocytes. The minor Yamaguchi criteria include: sore throat, lymphadenopathy, hepatomegaly or splenomegaly; abnormal liver studies, particularly elevations in aspartate and alanine aminotransferase and lactate dehydrogenase concentrations; negative tests for ANA and rheumatoid factor.

It is important to exclude the presence of any infection, malignancy or other rheumatic disorder as it precludes the diagnosis of AOSD. Our patient fulfilled nearly all the clinical and laboratory criteria required for the diagnosis of AOSD, namely the exclusion of other disorders. An extensive investigation was drawn to exclude infectious aetiologies. Nevertheless, an unidentified microorganism could be responsible for these manifestations and empirical antibiotherapy could have eradicated it. Although some clinical features attenuated during antibiotherapy, others, such as arthritis, had developed in the meantime. So we considered that an infectious agent was unlikely and started corticosteroids.

The presence of myopericarditis has seldom been reported.^{3 4} In this patient pericarditis was suggested by the pleuritic thoracic pain and the diffuse ST segment changes in the ECG, which did not follow any specific coronary territory and myocarditis was suggested also by the elevation of cardiac specific enzymes such as troponin T and CPK-MB.^{5 6} Later in the course, the cardiac MRI did not reveal any sequela.⁷

The aetiology of AOSD is unknown. A variety of infectious triggers have been suggested, including numerous viral pathogens. Suspected bacterial pathogens include *Yersinia enterocolitica* and *M. pneumoniae*. Usually there is a bimodal age distribution, with one peak between the ages of 15 and 25 years and the second between the ages of 36 and 46 years.² No trigger was identified in our patient.

Treatment of AOSD is not consensual. Although our patient had an apparent initial spontaneous remission, a high-dose corticosteroid was needed for the arthritis component and possibly for the cardiac involvement. In spite of the good response to corticosteroid treatment, methotrexate was required for full remission. In relapsing and resistant cases, intravenous human immunoglobulin and etanercept have been tried successfully, especially in relapses presenting as myopericarditis.⁸ Recent reports have suggested an important role for anti-interleukin (IL)-1 inhibitor anakinra in the management of AOSD.

Learning points

- ▶ Fever, rash and polyarthralgia is a syndrome with a wide range of differential diagnosis.
- ▶ Myopericarditis is a rare manifestation of adult-onset Still's disease (AOSD), which added to the difficulty of diagnosis.
- ▶ Corticosteroid therapy directed at AOSD is often delayed since it is an exclusion diagnosis.
- ▶ AOSD is difficult to manage given its remitting relapsing nature.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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